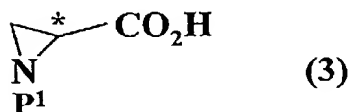
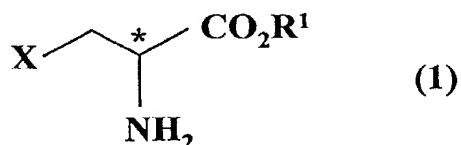


Claims

1. A process for producing an optically active N-protected-aziridine-2-carboxylic acid represented by the following formula (3):

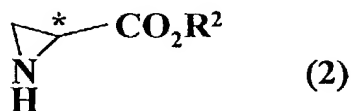


wherein * represents the position of an asymmetric carbon atom; and P¹ represents a benzenesulfonyl group substituted by nitro at the 2- and/or 4-positions; or its salt characterized by comprising subjecting an optically active 3-haloalanine derivative represented by the following formula (1):



wherein X represents a halogen atom; R¹ represents a hydrogen atom or a monovalent organic group which is involved in a structure represented by -CO₂R¹ and thus is capable of serving as an ester type protective group of a carboxyl group; and * is as defined above; to an intramolecular cyclization reaction in the presence of a base followed by, if needed, ester hydrolysis to give

an optically active aziridine-2-carboxylic acid derivative represented by the following formula (2):



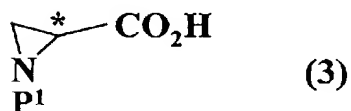
wherein * is as defined above; and R² has the same meaning as R¹ as defined above;

or its salt while maintaining the configuration at the 2-position, and then protecting the amino group followed by, if needed, ester hydrolysis.

2. The production process as claimed in claim 1, wherein P¹ in the formula (3) is a 2-nitrobenzenesulfonyl group or a 4-nitrobenzenesulfonyl group.

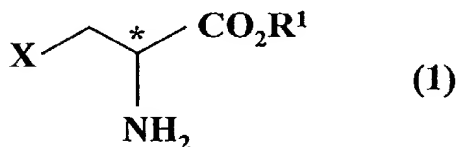
3. A production process as claimed in claim 1 or 2, wherein X in the formula (1) is a chlorine atom.

4. A process for producing an optically active N-protected-aziridine-2-carboxylic acid represented by the following formula (3):



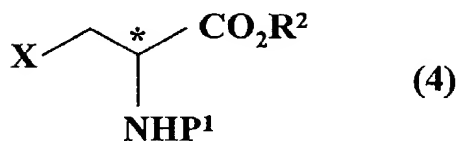
wherein P¹ and * are each as defined above;

or its salt characterized by protecting the amino group of an optically active 3-haloalanine derivative represented by the following formula (1):



wherein X, R¹ and * are each as defined above;

or its salt followed by, if needed, ester hydrolysis to give an optically active N-protected-3-haloalanine derivative represented by the following formula (4):



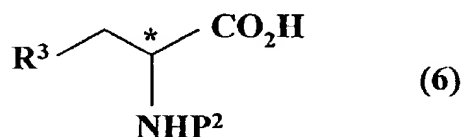
wherein X and * are each as defined above; R² has the same meaning as R¹ as defined above; and P¹ is the same as P¹ in the above formula (3);

or its salt, then subjecting it to an intramolecular cyclization reaction in the presence of a base followed by, if needed, ester hydrolysis.

5. The production process as claimed in claim 4, wherein X in the formula (1) is a chlorine atom.

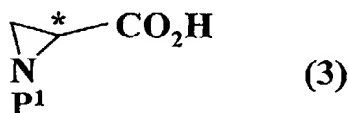
6. A production process as claimed in claim 4 or 5, wherein P^1 in the formula (4) is a 2-nitrobenzenesulfonyl group or a 4-nitrobenzenesulfonyl group.

7. A process for producing an optically active amino acid derivative represented by the following formula (6):



wherein R^3 represents an optionally substituted cyclic or noncyclic alkyl group having 1 to 30 carbon atoms, an optionally substituted aralkyl group having 7 to 30 carbon atoms, an optionally substituted aryl group having 6 to 30 carbon atoms, an optionally substituted alkenyl group having 2 to 30 carbon atoms, or an optionally substituted alkynyl group having 2 to 30 carbon atoms; and P^2 has the same meaning as P^1 as described above or represents a hydrogen atom;

or its salt characterized by comprising treating an optically active N-protected-aziridine-2-carboxylic acid represented by the following formula (3) which is produced by a method as claimed in any of claims 1 to 6:



wherein P¹ and * are each as defined above;
or its salt with an organic metal reagent represented by
the following formula (5):



wherein R³ is as defined above; and M represents an atomic
group containing an alkali metal atom or an alkaline earth
metal atom or an atomic group containing a zinc ion;
followed by, if needed, deblocking.

8. The production process as claimed in claim 7,
wherein M in the formula (5) is lithium, sodium, MgCl,
MgBr, ZnCl or ZnBr.

9. A production process as claimed in claim 7 or 8,
wherein said deblocking is performed with the use of a
thiol compound represented by the following formula (7):



wherein R⁴ represents an optionally substituted alkyl
group having 1 to 30 carbon atoms, an optionally
substituted aralkyl group having 7 to 30 carbon atoms, or
an optionally substituted aryl group having 6 to 30 carbon
atoms;

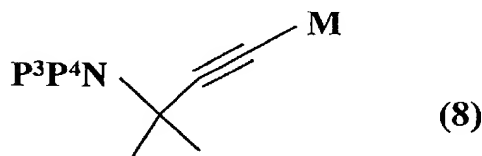
to give a compound represented by the formula (6) wherein
P² is a hydrogen atom.

10. The production process as claimed in claim 9, wherein said thiol compound represented by the formula (7) is thiophenol.

11. A production process as claimed in claim 7 or 8, wherein said deblocking is performed with the use of a metal alkoxide to give a compound represented by the formula (6) wherein P^2 is a hydrogen atom.

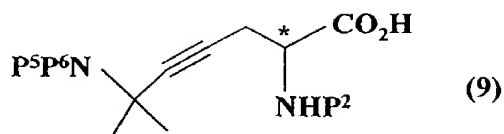
12. The production process as claimed in claim 11, wherein said metal alkoxide is an alkali metal alkoxide.

13. A production process as claimed in any of claims 7 to 12, wherein a metal acetylide represented by the following formula (8):



wherein M is as defined above; and P^3 and P^4 independently represent each a hydrogen atom or an amino-protective group, or P^3 and P^4 form together an amino-protective group;

is used as said organic metal reagent represented by the formula (5) to give an optically active amino acid derivative represented by the following formula (9):



wherein P⁵ and P⁶ independently have the same meanings as P³ and P⁴ as described above; P² has the same meaning as P² as defined in the above formula (6); and * represents the position of an asymmetric carbon atom; or its salt as the compound represented by the formula (6).

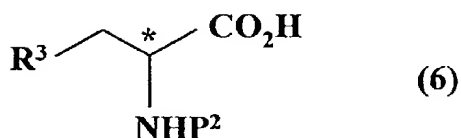
14. The production process as claimed in claim 13, wherein said metal acetylide represented by the formula (8) is prepared by treating an optionally protected 3,3-dimethylpropargylamine represented by the following formula (10):



wherein P³ and P⁴ are each as defined above;
with at least one member selected from among organic
lithium, organic lithium amide, a Grignard reagent and
organic magnesium amide.

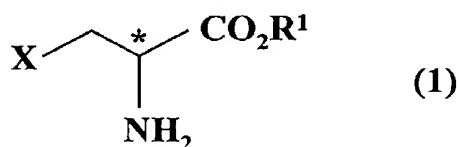
15. A production process as claimed in claim 13 or 14, wherein P^3 and P^4 in the formulae (8) and (10) respectively represent a hydrogen atom and a benzyl group.

16. A process for producing an optically active amino acid derivative represented by the following formula (6):



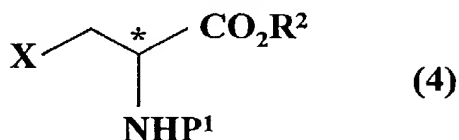
wherein R^3 and P^2 are each as defined above;

or its salt characterized by comprising protecting the amino group of an optically active 3-haloalanine derivative represented by the following formula (1):



wherein X , R^1 , $*$ are each as defined above;

or its salt followed by, if needed, ester hydrolysis to give an optically active N-protected-3-haloalanine derivative represented by the following formula (4):



wherein X , R^2 and $*$ are each as defined above;

or its salt, and then treating it with an organic metal reagent represented by the following formula (5):



wherein R^3 is as defined above;

followed by, if needed, deblocking and/or ester hydrolysis.

17. The production process as claimed in claim 16, wherein X in the formula (1) is a chlorine atom.

18. A production process as claimed in claim 16 or 17, wherein M in the formula (5) is lithium, sodium, MgCl, MgBr, ZnCl or Zn Br.

19. A production process as claimed in any of claims 16 to 18, wherein said deblocking is performed with the use of a thiol compound represented by the following formula (7):



wherein R^4 is as defined above;

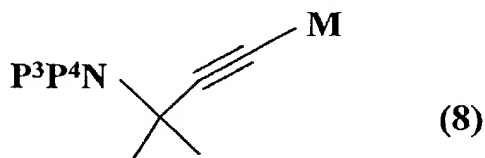
to give a compound represented by the formula (6) wherein P^2 is a hydrogen atom.

20. The production process as claimed in claim 19, wherein said thiol compound represented by the formula (7) is thiophenol.

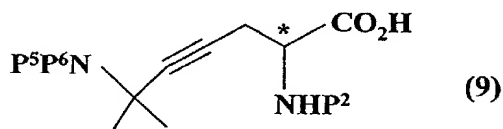
21. A production process as claimed in any of claims 16 to 18, wherein said deblocking is performed with the use of a metal alkoxide to give a compound represented by the formula (6) wherein P^2 is a hydrogen atom.

22. The production process as claimed in claim 21, wherein said metal alkoxide is an alkali metal alkoxide.

23. A production process as claimed in any of claims 16 to 22, wherein a metal acetylide represented by the following formula (8):



wherein M, P³ and P⁴ are each as defined above;
is used as said organic metal reagent represented by the formula (5) to give an optically active amino acid derivative represented by the following formula (9):



wherein P², P⁵, P⁶ and * are each as defined above;
or its salt as the compound represented by the formula (6).

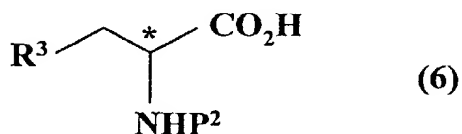
24. The production process as claimed in claim 23, wherein said metal acetylide represented by the formula (8) is prepared by treating an optionally protected 3,3-dimethylpropargylamine represented by the following formula (10):



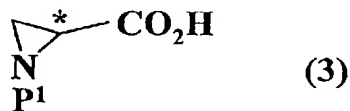
wherein P³ and P⁴ are each as defined above;
with at least one member selected from among organic lithium, organic lithium amide, a Grignard reagent and organic magnesium amide.

25. A production process as claimed in claim 23 or 24, wherein P³ and P⁴ in the formula (8) respectively represent a hydrogen atom and a benzyl group.

26. A process for producing an optically active amino acid derivative represented by the following formula (6):



wherein R³, P² and * are each as defined above;
or its salt characterized by comprising treating an optically active N-protected aziridine-2-carboxylic acid represented by the following formula (3):



wherein P¹ and * are each as defined above;

or its salt with an organic metal reagent represented by the following formula (5):



wherein R^3 and M are each as defined above;
followed by, if needed, deblocking.

27. The production process as claimed in claim 26, wherein M in the formula (5) is lithium, sodium, MgCl, MgBr, ZnCl or ZnBr.

28. A production process as claimed in claim 26 or 27, wherein said deblocking is performed with the use of a thiol compound represented by the following formula (7):



wherein R^4 is as defined above;
to give a compound represented by the formula (6) wherein P^2 is a hydrogen atom.

29. The production process as claimed in claim 28, wherein said thiol compound represented by the formula (7) is thiophenol.

30. A production process as claimed in claim 26 or 27, wherein said deblocking is performed with the use of a metal alkoxide to give a compound represented by the formula (6) wherein P^2 is a hydrogen atom.

31. The production process as claimed in claim 30, wherein said metal alkoxide is an alkali metal alkoxide.

Year	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100
1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	


$$\text{P}^5\text{P}^6\text{N} \text{---} \text{C} \text{---} \text{C} \text{---} \text{C}^* \text{---} \text{CO}_2\text{H} \quad \text{NHP}^2 \quad (9)$$

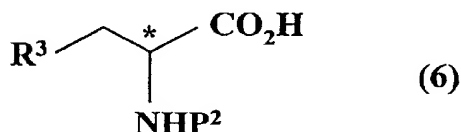
33. The production process as claimed in claim 32, wherein said metal acetylide represented by the formula (8) is prepared by treating an optionally protected 3,3-dimethylpropargylamine represented by the following formula (10):



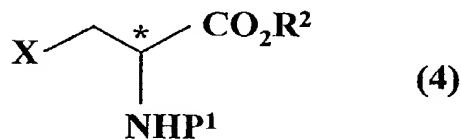
wherein P^3 and P^4 are each as defined above;
 with at least one member selected from among organic
 lithium, organic lithium amide, a Grignard reagent and
 organic magnesium amide.

34. A production process as claimed in claim 32 or
 33, wherein P^3 and P^4 in the formula (8) respectively
 represent a hydrogen atom and a benzyl group.

35. A process for producing an optically active
 amino acid derivative represented by the following formula
 (6):



wherein R^3 and P^2 are each as defined above;
 or its salt characterized by comprising treating an
 optically active N-protected-3-haloalanine derivative
 represented by the following formula (4):



wherein X, R^2 , P^1 and * are each as defined above;

or its salt with an organic metal reagent represented by the following formula (5):



wherein R^3 and M are each as defined above;
followed by, if needed, deblocking and/or ester hydrolysis.

36. The production process as claimed in claim 35, wherein X in the formula (4) is a chlorine atom.

37. A production process as claimed in claim 35 or 36, wherein M in the formula (5) is lithium, sodium, MgCl, MgBr, ZnCl or Zn Br.

38. A production process as claimed in any of claims 35 to 37, wherein said deblocking is performed with the use of a thiol compound represented by the following formula (7):



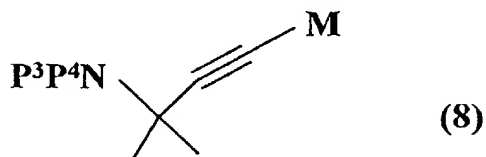
wherein R^4 is as defined above;
to give a compound represented by the formula (6) wherein P^2 is a hydrogen atom.

39. The production process as claimed in claim 38, wherein said thiol compound represented by the formula (7) is thiophenol.

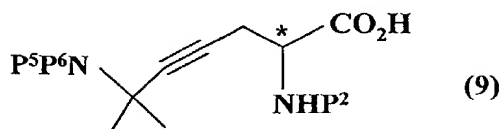
40. A production process as claimed in any of claims 35 to 37, wherein said deblocking is performed with the use of a metal alkoxide to give a compound represented by the formula (6) wherein P^2 is a hydrogen atom.

41. The production process as claimed in claim 40, wherein said metal alkoxide is an alkali metal alkoxide.

42. A production process as claimed in any of claims 35 to 41, wherein a metal acetylide represented by the following formula (8):



wherein M, P³ and P⁴ are each as defined above; is used as said organic metal reagent represented by the formula (5) to give an optically active amino acid derivative represented by the following formula (9):



wherein P², P⁵, P⁶ and * are each as defined above; or its salt as the compound represented by the formula (6).

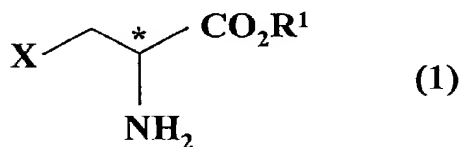
43. The production process as claimed in claim 23, wherein said metal acetylide represented by the formula (8) is prepared by treating an optionally protected 3,3-dimethylpropargylamine represented by the following formula (10):



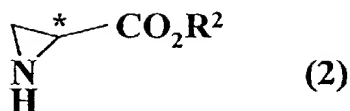
wherein P^3 and P^4 are each as defined above;
with at least one member selected from among organic lithium, organic lithium amide, a Grignard reagent and organic magnesium amide.

44. A production process as claimed in claim 42 or 43, wherein P^3 and P^4 in the formula (8) respectively represent a hydrogen atom and a benzyl group.

45. A process for producing an optically active aziridine-2-carboxylic acid derivative or its salt which comprises using an optically active 3-haloalanine derivative represented by the following formula (1):



wherein X, R^1 and * are each as defined above;
or its salt in the presence of a base to give an optically active aziridine-2-carboxylic acid derivative represented by the following formula (2):

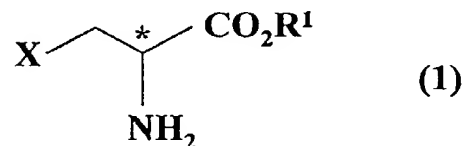


wherein R^2 and $*$ are each as defined above;
 or its salt, characterized by, using an alkali metal hydroxide or an alkaline earth metal hydroxide as the base, performing an intramolecular cyclization reaction in the presence of water at a temperature of 70°C or higher followed by, if needed, ester hydrolysis.

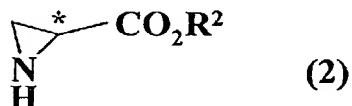
46. The production process as claimed in claim 45, wherein said base is an alkali metal hydroxide.

47. A production process as claimed in claim 45 or 46, wherein said optically active 3-haloalanine derivative or its salt is added to a mixture containing water and a base.

48. A process for producing an optically active aziridine-2-carboxylic acid derivative or its salt which comprises using an optically active 3-haloalanine derivative represented by the following formula (1):



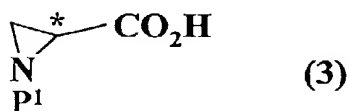
wherein X, R¹ and * are each as defined above;
or its salt in the presence of a base to give an optically active aziridine-2-carboxylic acid derivative represented by the following formula (2):



wherein R² and * are each as defined above;
or its salt, characterized by, using an amine as the base, performing an intramolecular cyclization reaction followed by, if needed, ester hydrolysis.

49. The production process as claimed in claim 48, wherein said amine is an aliphatic amine.

50. A process for producing an optically active N-protected-aziridine-2-carboxylic acid represented by the following formula (3):



wherein P¹ and * are each as defined above;
or its salt characterized by comprising treating an optically active aziridine-2-carboxylic acid derivative

[illegible]

51. An optically active N-protected-aziridine-2-carboxylic acid represented by the following formula (3):



52. A compound as claimed in claim 51, wherein P¹ is a 2-nitrobenzenesulfonyl group or a 4-nitrobenzenesulfonyl group.

$$\text{P}^5\text{P}^6\text{N} \text{---} \text{C} \equiv \text{C} \text{---} \text{CH}(\text{NHP}^2) \text{---} \text{CO}_2\text{H} \quad (9)$$

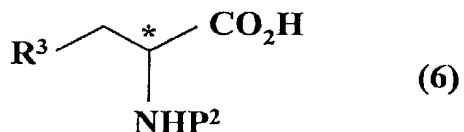
wherein P², P⁵, P⁶ and * are each as defined above;
or its salt.

54. A compound as claimed in claim 53, wherein P² is a 2-nitrobenzenesulfonyl group or a 4-nitrobenzenesulfonyl group.

55. A compound as claimed in claim 53, wherein P² is a hydrogen atom.

56. A compound as claimed in any of claims 53 to 55, wherein P⁵ is a hydrogen atom and P⁶ is a benzyl group.

57. A process for crystallizing a compound represented by the following formula (6):



wherein R³ is as defined above;
characterized by comprising neutralizing with an acid an aqueous solution containing an N-protected optically active amino acid derivative salt represented by the formula (6) wherein P² is a 2-nitrobenzenesulfonyl group or a 4-nitrobenzenesulfonyl group and thus crystallizing to thereby give the compound of the formula (6) in free state.

58. The crystallization process as claimed in claim 57, wherein said N-protected amino acid derivative salt is an alkali metal salt.

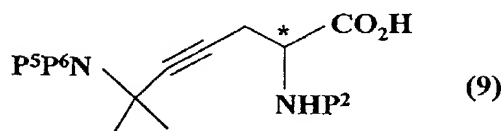
59. The crystallization process as claimed in claim 58, wherein said alkali metal salt is a lithium salt.

60. A crystallization process as claimed in any of claims 57 to 59, wherein said acid is a halogenated hydroacid.

61. The crystallization process as claimed in claim 60, wherein said halogenated hydroacid is hydrogen chloride.

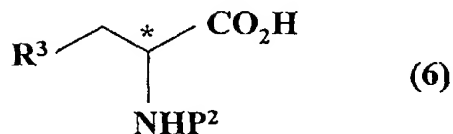
62. A crystallization process as claimed in any of claims 57 to 61, wherein the reaction is performed in the coexistence of an organic solvent compatible with water.

63. A crystallization process as claimed in any of claims 57 to 62, wherein said compound represented by the formula (6) is an N-protected optically active amino acid derivative salt represented by the following formula (9):



wherein P^2 represents a 2-nitrobenzenesulfonyl group or a 4-nitrobenzenesulfonyl group; and P^5 , P^6 and $*$ are each as defined above.

64. A process for crystallizing a compound represented by the following formula (6):



wherein R³ is as defined above;

characterized by comprising salting out with a halogenated alkali metal salt an aqueous solution containing an alkali metal salt of an optically active amino acid derivative represented by the formula (6) wherein P² is hydrogen atom to thereby give an alkali metal salt of the compound (6).

65. The crystallization process as claimed in claim 64, wherein said alkali metal salt of an optically active amino acid derivative is a lithium salt.

66. A crystallization process as claimed in claim 64 or 65, wherein said halogenated alkali metal salt is lithium chloride.

67. A crystallization process as claimed in any of claims 64 to 66, wherein the reaction is performed in the coexistence of an organic solvent compatible with water.

68. A crystallization process as claimed in any of claims 64 to 67, wherein said compound represented by the formula (6) is an optically active amino acid derivative salt represented by the following formula (9):

$$\text{P}^5\text{P}^6\text{N} \begin{array}{c} \diagup \\ \diagdown \end{array} \text{---} \text{C} \equiv \text{C} \text{---} \text{CH}^* \text{---} \text{CO}_2\text{H} \quad \text{NHP}^2 \quad (9)$$

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